THEORETICAL STUDY ON THE METAL CATALYZED REARRANGEMENT OF CYCLOPROPANE DERIVATIVES IN AMBIENT CONDITION.

SYNOPSIS ON THE PROPOSED AREA OF RESEARCH
RELATED TO Ph.D (SCIENCE)

By

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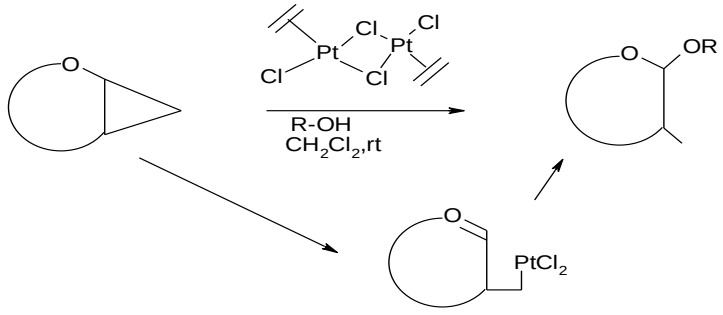
Synopsis

Chemists are able to do research more efficiently if they have a model for understanding the chemistry. Rearch on the study of stereoselective organic reactions ad its applications for synthesizing different target molecules is probably an important site for illustrations. To rationalize the stereoselectivity for a stereoisomeric product in a stereoselective reaction, it is a common practice to use some models of the possible transition states and work out various interacting forces to determine their stability. Thus, molecular modeling is necessary to determine the actual reaction mechanisms as well as the composition of reaction product of stereoselective reactions.

In this report we have theoretically investigated on the mechanism of some rearrangement reactions in cycloproane derivatives catalyzed by a metal.

- **Origin of the research problem**

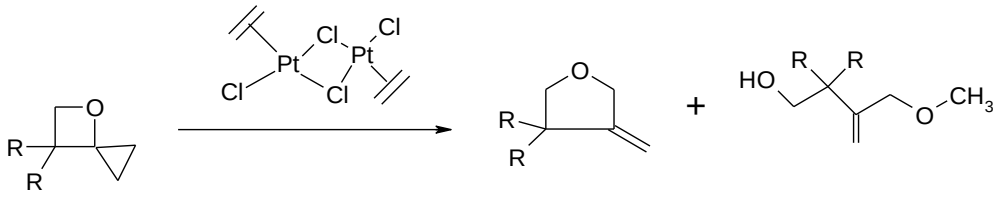
Strained nature in cyclopropane ring system makes it a suitable substrate for many facile reactions, though the theoretical study on all these processes has not been explored with full clarity. Action of the metal for opening of three membered ring have been attracting a great deal of interest of many theoretical and practical researchers for a long time. Reports of the action of Zeise's dimer on silyloxy-cyclopropanes[1] and alkoxycyclopanes[2] reveal a mechanism that involves the oxidative addition of platinum into cyclopropane next to the CO bond to generate an oxocarbenium[3] intermediate. Another report of the ring opening reaction of 1,2 cyclopropanated sugars[4] that gives C2–substituted glycoside under the catalysis of Zeise's dimer in alcoholic medium has also been explained by assuming the formation of an oxo-carbenium ion intermediate (Scheme-1).



Scheme-1

Recently a report from the Howell and his group[5] shows that the oxaspirohexane derivative gives a mixture of two products, 3-methylene tetrahydrofuran and allyl ether under similar

condition (scheme-2). As these outcomes couldn't be rationalized by the oxocarbenium intermediates the authors suggest another mechanism involving the insertion of metal ion in ring system (Scheme-2).



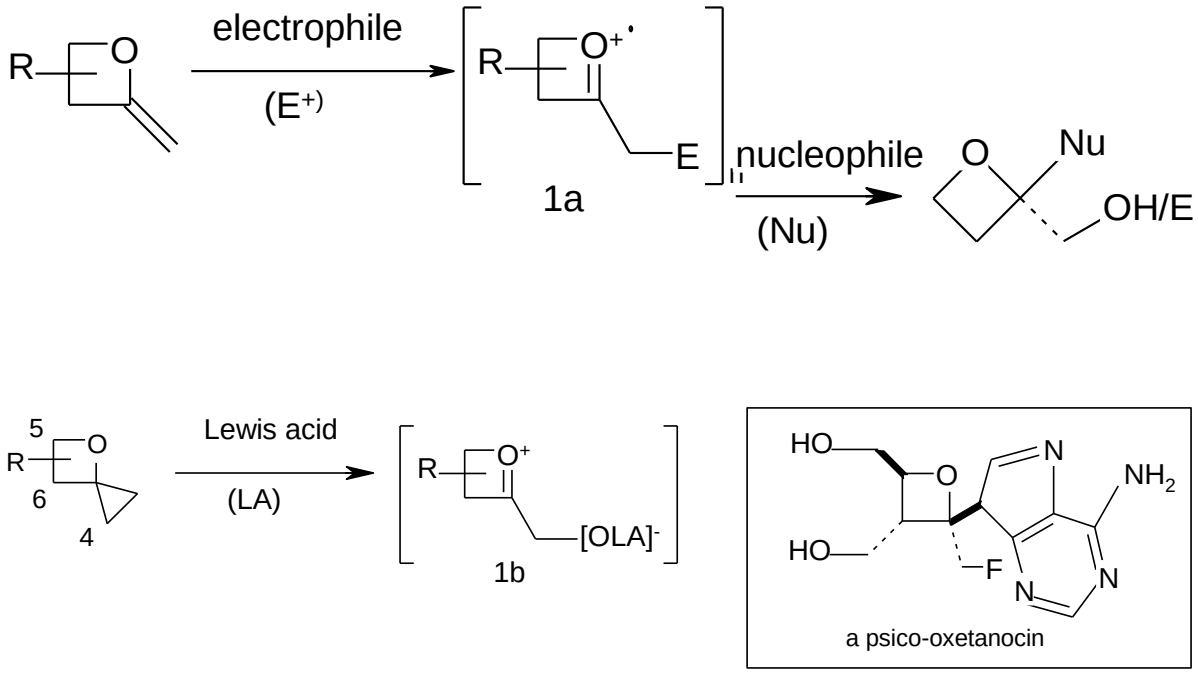
Scheme-2

Using ^{13}C–labelling experiments they showed that the mechanism involves the oxidative addition of metal atom regioselectively to the C-C bond bearing least substituents to form a platina cyclobutane intermediate.

Though all the mechanism have been derived from chemical intuition supported by several experimental outcomes, a rigorous theoretical investigation is required for the final confirmation of the actual pathway. Our plan is to investigate two separate pathways involving either the formation of oxocarbenium ion or the formation of platinacyclobytane intermediate. For such investigation we employ the most widely accepted density functional theory implemented in Gaussian software.

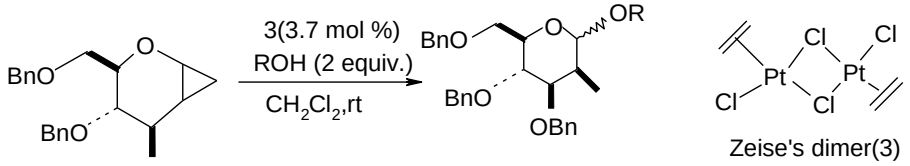
- **<u>Objective of the work</u>**

Our objective is to investigate the mechanism of Pt (II) catalysed ring opening reactions of several fused and free cyclopropane ring system. Before stating the actual problem it is necessary to correlate our plan with previous Pt catalysed rearrangement studies so far. Previous report shows that preparation of oxaspirohexanes[6] from methyleneoxetanes[7] and its new reactivity's (Scheme-3).



Scheme 3: Routes to oxetane intact products from methyleneoxetanes or dioxaspirohexan-es through oxocarbenium ions **1a** or **1b**.

Our attention was captured by reports from Madsen and co-workers that 1,2-cyclopropanated sugars gave C2-substituted glycosides 2 when reacted with alcohols in the presence of Zeise's dimer, $[Pt(C_2H_4)Cl_2]_2$ (3) (Figure 2)[8]. From these results and prior reports of the reaction of Zeise's dimer with silyloxycyclopropanes[9] and alkoxycyclo-propanes,[10] a mechanism involving oxidative addition of platinum into the cyclopropane next to the CO bond to give an oxocarbenium ion[4a] was proposed(Figure 2). On the basis of these Madsen results, it was postulated that oxaspirohexanes **4** could be converted to psico-nucleosides **5** with Zeise's dimer insertion into the cyclopropane providing an alternative access to oxetaneoxocarbenium ions.



proposed intermediate:

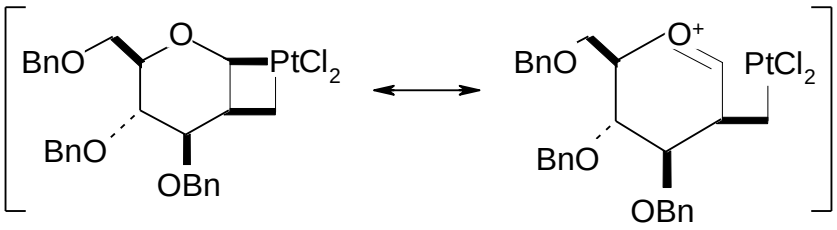
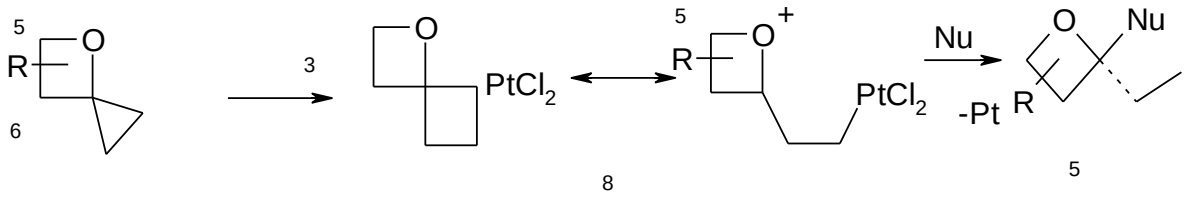
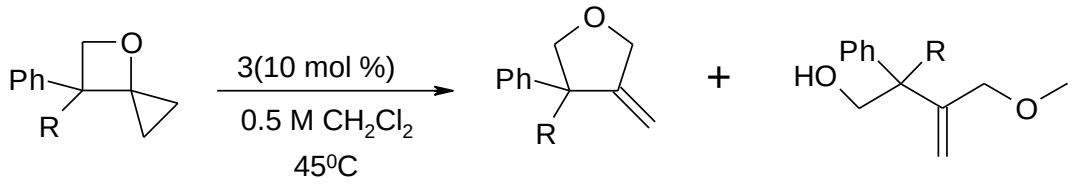


Figure 2. Madsen Zeise's dimer-catalyzed ring-opening of 1,2-cyclopropanated sugurs.[4]



Scheme 4: Anticipated transformation of oxaspirohexanes **4** in the presence of **3** to give novel psico-nucleosides **5**

Unexpectedly, under the Madsen conditions,[4] oxaspirohexane **4a** (or **4b**) gave mixtures of two products, 3-methylenetetrahydrofuran **6a** (or **6b**) and allyl ether **7a** (or **7b**) (Scheme 5). Moreover, in the absence of MeOH, **4a** was converted to just 3-methylenetetrahydrofuran **6a**, while allyl ether **7a** was the sole isolable product in the presence of excess MeOH. Neither outcome could be rationalized by oxocarbeniumions like **8** (Scheme 4). Thus, these initial results represented a novel pathway for reactions between oxygen-substituted cyclopropanes and Zeise's dimer.



4a R= H
4b= CH_3

6a/b

7a/b

Scheme 5: Initial Findings on the Reaction of oxaspirohexanes with Zeise's Dimer

METHODLOGY

- **Computational methods**

Methods of calculation:- For the computational modelling of the proposed project work, both Molecular Mechanical (MM) and Quantum Mechanical (QM) methods will be adopted. The geometry optimization and energy calculation of all the systems will be performed by using Gaussian 09[11] software and also for the visualization of the output files some graphics software like gauss view[12], Molden[13], Gabedit[14] VMD etc will be used.

For most of the cases we will be employed Density Functional Theory (DFT) method for the saddle point calculation. B3LYP hybrid functional and 6-31G* basis set will be used for this purpose.In most of the cases Cartesian Coordinates will be used to optimize the geometry. For optimization of ground state geometry the Fletcher-Powell(FP) algorithm will be used.

The most important task of this modelling will be the exploration of the potential energy surface (PES) of the molecular assembly involved in the reactions. The potential energy surface is the most complete description of all the conformers, isomers and energetically accessible motions of a molecular system. Our special interest is to locate the stationary points on the potential energy surface. Most informative stationary points are the minima and the saddle points. Minima on the potential energy surface (PES) correspond to the optimized geometries. The lowest energy minimum is called global minimum. The transition structure between the reactant and product of a reaction is a saddle point on this structure. All the species, like reactant, product and transition state linking these two, are called stationary points. At the stationary point the surface is parallel to the horizontal line corresponding to one geometric parameter or to the plane corresponding to two geometric parameters or to a hyper plane corresponding to more than two geometric parameters. Hence, the first derivative of the potential energy with respect to each geometric parameter is zero i.e. $\frac{\delta E}{\delta q} = 0$ However, a minima is a minimum all directions, but a saddle point is a maximum along the reaction coordinate and a minimum all other directions. They can be distinguished by the second derivative of energy with respect to the nuclear coordinates. Mathematically it can be written as, at the minimum, $\frac{\delta 2E}{\delta q 2} > 0$ for all values of q, at the saddle point, $\frac{\delta 2E}{\delta q 2} > 0$ for all q except, along the reaction coordinate. Along the reaction coordinate, $\frac{\delta 2E}{\delta q 2} < 0$. A PES can be used to find both the saddle points and the reaction co-ordinates.

Calculation of the electrostatic potential surface (PES) of the molecular assembly under investigation will also be studied to explore the electrostatic effect operating in the transition structure of the correcponding reaction.

- **Future prospect**

Considering all the reported experimentral and preliminary theoretical investigation it may be concluded that the mechanism of reaction pathway of the Pt-Catalyzed Ring opening of spirocyclopentane oxa-butane derivative describes several features such as: activation energy, stereoselectivity which is related to the process. We hope that all these works of us will give successful results and our proposed pathways.

We also believe that the outcome of our theoretical investigations will give a new idea about the reaction mechanism of the cyclopropane ring opening reaction for the formation of spirocyclopentane oxa-butane.

- **References**

[1](a) Ikura,K.,Ryu,I.,Kambe,N.,Sonoda,N.J.Am. Chem.Soc. 1992, 114,1520. (b) For a review involving Zeise's dimer-catalyzed isomerization of siloxycyclopropanes: Sugimura, T., Ryu, I. J. Synth. Org. Chem., Jpm. 2000,58,1100.

[2]Hoberg, J.O.,Jennings, P.W. Oraganometallics 1996,15,3902.

[3]Beyer, J.,Skaanderup, P. R; Madsen, R. J.Am. Chem.. Soc.2000,122,9575.

[4]Beyer, J.,Madsen, R. J. Am. Chem. Soc. 1998,120,12137.

[5]Malapit, C. A., Chaitale.S.M., Thakur. M. S., Taboada. R., Howell. A. R., Org. Chem. 2015, 80, 5196-5209.

[6] (a) Liang, y.; Hnatiuk, N.; Rowley, M.; Whiting, B. T.; Coates, G. W.; Rablen, P. R.; Morton, M.; Howell, A.R. J. Org. Chem. 2011, 76, 9962.

(b) Dollinger, L. M.; Ndakala, A. J.; Hashemzadeh, M.; Wang, G.; Wang, Y.; Martinez, I.; Arcari, J. T.; Galluzzo, D. J.; Howell, A. R.; Reheingold, A. L.; Figuero, J.S. J. Org. Chem. 1999, 64,7074.

(c) Wang., G.; Wang, Y.; Arcari, J. T.; Howell, A. R.; Rehingold, A. L.; Concollino, T. Tetrahedron Lett. 1999, 40, 7051.

[7] (a) Keshipeddy, S.; Martinez, I.; Castillo, B.F.; Morton, M.D.; Howell, A. R. J. Org. Chem. 2012, 77, 7883.

(b) Blauvelt, M. L.; Howell, A. R. J. Org. Chem. 2008, 73,517.

(c) Taboada, R.; Ordonio, G. G.; Ndakala. A. J.; Howell, A. R.; Rablen, P. R. A. J. Org. Chem. 2003, 68, 1480.

[8] (a) Beyer, J.; Madsen, R. J. Am. Chem. Soc. 1998, 120,12137.

(b) Beyer, J..; Skaanderup, P. R.; Madsen, R. J. Am. Chem. Soc. 2000, 122, 9575.

[9] (a) Ikura, K.; Ryu, I.; Kambe, N.; Sonoda, N. J. Am. Chem. Soc. 1992, 114, 1520.

(b) For a review involving Zeise's dimer-catalyzed isomerization of siloxycyclopropanes: Sugimura, T.; Ryu, I. J. Synth. Org. Chem. Jpn. 2000, 58, 1100.

[10] Hoberg, J. O.; Jennings, P.W. Organometallics 1996, 15, 3902.

[11] Official Gaussian Website: http://www.gaussian.com

[12]Official Gaussian Website: http:// www.gaussian.com

[13]Schaftennar, G.; Noordik, H., J. Comput Aided Mol. Des., 14, 2000,123.

[14]A.R.Allouche, Official gabeditWebsite:http//gabedit. Sourceforge.net